Reminder of important clinical lesson

Bronchiolitis obliterans organising pneumonia syndrome presenting with neutrophilia in bronchoalveolar lavage fluid after breast-conserving therapy

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Summary

A 61-year-old female presented with a dry cough and fever 4 months after tangential radiation therapy (RT) following conserving surgery for breast cancer. Chest radiography and CT demonstrated consolidation with air bronchogram outside the irradiated area. Neutrophil granulocytes were abundant in bronchoalveolar lavage fluid (BALF) (39.6% of total cells), and transbronchial lung biopsy revealed organising pneumonia (OP) histologically. Antibiotic therapy had no effect, but corticosteroid therapy brought about clinical improvement. Her condition was diagnosed as bronchiolitis obliterans OP (BOOP) syndrome. Lymphocytic BALF has been identified as a characteristic of BOOP syndrome induced after RT for breast cancer. The BALF in this case, however, was neutrophilic. In our analysis of differential cell counts in the BALF of 24 patients with BOOP syndrome, the BALF was neutrophilic (>5%) in 16 (76%) cases, and the neutrophilia was severe in some of those patients.

BACKGROUND

Reports of bronchiolitis obliterans organising pneumonia (BOOP) occurring in women after radiation therapy (RT) for breast cancer have shown that radiation to the lung can induce OP. This clinical condition is called BOOP syndrome. The literature has shown lymphocytosis to be a characteristic finding in the bronchoalveolar lavage fluid (BALF) of patients with BOOP syndrome. This report is of special interest because the patient presented with neutrophilia in BALF.

CASE PRESENTATION

A 61-year-old female, a housewife who had never smoked, was admitted to our hospital because of fever and dry cough. She had received a right partial mastectomy for breast cancer 8 months before admission, followed by 50 gray of adjuvant tangential irradiation 2 months later. Anastrozole was commenced when the radiotherapy was administered. She developed fever and dry cough 1 month before admission, and a chest radiograph revealed an infiltrative shadow in the right upper zone. She received garenoxacin for 1 week at that point, but her symptoms and abnormal lung shadow remained unchanged. Her vital signs on admission were a temperature of 37.2°C, blood pressure of 123/86 mm Hg, pulse of 117 beats per min with regular rhythm and oxygen saturation of 97% on pulse oximetry (SpO₂). Fine crackles in the upper right lung were detected on auscultation, and cardiac sound indicated a regular rhythm with no heart murmur.

INVESTIGATIONS

Elevated levels of C reactive protein (7.37 mg/dl) were noted in the laboratory data. Clear evidence of liver dysfunction was also found (aspartate aminotransferase, 45 U/l; alanine aminotransferase, 53 U/l; lactate dehydrogenase,

221 U/l; alkaline phosphatase, 1178 U/l), presumably in association with the garenoxacin therapy. Various autoantibodies were negative. KL-6 and surfactant protein-D, markers of interstitial lung disease, were within normal limits. Chest radiograph revealed an infiltrative shadow in the right upper and middle lung zone (figure 1A). Chest CT showed air space consolidation surrounded by ground glass opacity. The shadow was located outside of the irradiated area (figure 1B).

BALF analysis revealed marked neutrophilia (39.6%) and mild lymphocytosis (19.5%). No malignant cells were detected and no microorganisms were cultured in BALF. The specimens from transbronchial lung biopsy revealed OP manifesting intraalveolar organisation (figure 1C).

DIFFERENTIAL DIAGNOSIS

Fever, inflammation and radiological evidence of peripheral airspace consolidation in patients who undergo breast-conserving therapy followed by RT are suggestive of BOOP syndrome.

Neutrophilia in BALF usually indicates a disorder associated with bacterial infection.

When administered over a course of several months, anastrozole is one of the drugs known to cause drug-induced OP.

TREATMENT

Therapy was initiated with prednisolone at 0.5 mg/kg per day, and the prednisolone dose was gradually tapered.

OUTCOME AND FOLLOW-UP

Her symptoms and laboratory findings resolved promptly after prednisolone administration commenced, and the infiltrative shadow on radiography gradually improved.

Figure 1 (A) Chest radiograph shows infiltrative shadow in the right upper and middle lung zone. (B) Chest CT shows air space consolidation surrounded by ground glass opacity. The shadow is located outside the irradiated area (arrow). (C) Pathological specimens from transbronchial lung biopsy showing intraalveolar organisation and slight interstitial inflammation (H&E staining). (D) The dot plot shows our analysis of bronchoalveolar lavage fluid (BALF) in 24 patients with bronchiolitis obliterans organising pneumonia syndrome after radiation therapy. The Y axis represents the percentage of neutrophils in BALF. The arrow indicates the present case. The bar indicates mean $\pm$ SD.

DISCUSSION

Breast-conserving therapy followed by RT has recently become a standard treatment for early breast cancer.^{1 2} In 1995, Bayle *et al* reported a series of cases with OP primed by RT for breast cancer,³ a condition they described as ‘radiation-induced BOOP syndrome.’ Crestani *et al* reported the following diagnostic criteria for BOOP syndrome in a review of 15 cases: (1) RT to the breast for carcinoma within 12 months; (2) general and/or respiratory symptoms lasting for at least 2 weeks; (3) radiographic lung infiltrates outside the radiation area; and (4) no evidence of a specific cause. Our patient fulfilled all of these criteria.⁴ The major symptoms of BOOP syndrome are generally cough (83%) and fever (91%), but some patients are asymptomatic (8%). Almost all patients who develop radiation-induced BOOP syndrome do so within 6 months of the RT.⁵ The incidence is 1.8%.⁶ Corticosteroids are the current standard treatment. Corticosteroids brought about dramatic improvement in all of the 15 cases reported by Crestani *et al*, but relapses occurred in 80% of those cases when the corticosteroids were tapered or stopped. Crestani *et al* also analysed BALF findings in 10 patients with BOOP syndrome.⁴ All 10 of them had lymphocytosis greater than 20%, eight of them exhibited neutrophilia (>5%), and five of them exhibited eosinophilia (>5%). Another paper reported a marked increase in the percentage of lymphocytes ($36\% \pm 5.4\%$), along with mild increases in the percentages of neutrophils ($3.8\% \pm 1.2\%$) and eosinophils ($2.4\% \pm 1\%$).⁷ Our group analysed the cell counts in BALF of 24 patients with BOOP syndrome: 13 cases treated at St Luke’s International Hospital, 10 patients reported in the Japanese literature, and our case. Sixteen (76%) of these cases were neutrophilic (>5%) (figure 1D), and the neutrophilia was marked in the BALF of some of those patients. We concluded that neutrophilia is sometimes seen in the BALF analysis of BOOP syndrome after RT.

Learning points

- ▶ Non-segmental air-space consolidation in patients who have undergone RT after breast-conserving therapy is suggestive of BOOP syndrome.
- ▶ The major symptoms are cough and fever. Almost all patients who develop the syndrome do so within 6 months after radiotherapy.
- ▶ Corticosteroids are the current effective treatment, but the patients frequently relapse when the corticosteroids are tapered or stopped.
- ▶ Neutrophilia is sometimes seen in the BALF analysis of BOOP syndrome. We should therefore keep BOOP syndrome in mind as a differential diagnosis for patients who manifest an infiltrative shadow compatible with OP after receiving RT, even if they are neutrophilic in BALF analysis.

Competing interests None.

Patient consent Obtained.

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